IB/04/03872

THE PATENTS ACT, 1970

It is hereby certified that annexed hereto is a true copy of Application & Complete Specification filed in respect of Patent Application No.964/CHE/2003, dated 25/11/2003 by M/s. AUROBINDO PHARMA LIMITED, at Plot No.2, Maitrivihar Complex (Regd. Office), Ameerpet, Andhra Pradesh, Hyderabad – 500 038, India.

.....

PRIORITY DOCUMENT
SUBMITTED OR TRANSMITTED IN COMPLIANCE WITH RULE 17.1(a) OR (b)

.....In witness thereof

I have hereunto set my hand

Dated this the 9th February, 2005
20th day Magha, 1926 (Saka)

M.S. V

(M.S. VENKATARAMAN)
ASSISTANT CONTROLLER OF PATENTS & DESIGNS

FICE BRANCH
MENT OF INDIA
Guna C plex, 6th Floor, Annex.II
No.443, na Salai, Teynampet, Chennai – 600 018.

FORM 1

THE PATENTS ACT, 1970
(39 of 1970)
APPLICATION FOR GRANT OF A PATENT OFFICE
[See section 5(2), 7/54 and 135]

1. We,

AUROBINDO PHARMA LIMITED
PLOT NO. 2, MAITRIVIHAR COMPLEX (Regd. Office)
AMEERPET
ANDHRA PRADESH
HYDERABAD – 500 038
INDIA
AN INDIAN ORGANISATION

2. Hereby declare: -

(a) That we are in possession of an invention titled:

(b) **"PHARMACEUTICAL COMPOSITIONS OF ANHYDROUS MIRTAZAPINE."**

(c) That the Complete Specification relating to this invention is filed with this application.

(d) That there is no lawful ground of objection to grant of a Patent to us.

3. Further declare that the inventor(s) for the said invention is: -

(a) **ALURI PHANINDRUDU**

(b) **ASHISH GOGIA**

C/o. AUROBINDO PHARMA LIMITED
PLOT NO. 2, MAITRIVIHAR COMPLEX (Regd. Office)
AMEERPET
ANDHRA PRADESH
HYDERABAD – 500 038.
INDIA

(a) to (c) : **CITIZENS OF INDIA**

4. We claim the priority from the application(s) filed in convention countries, particulars of which are as follows:-
(a) NIL
(b) NONE

5. We state that the said invention is an improvement in or modification of the particulars of which are as follows and of which we are the Applicant/Patentee:

(a) NIL

(b) NONE

6. We state that the application is divided out of our application, the particulars of which are given below and pray that this application be deemed to have been filed on .... under section 16 of the Act:

NONE

7. That we are the assignee of the true and first Inventors.

8. That our addresses for service in India is as follows:

AUROBINDO PHARMA ITD
Plot No. 2, Maitrivihar Complex, (Regd Office)
Ameerpet,
Andhra Pradesh
Hyderabad - 500 038
India
Phone No.: 91-40-23741083
Fax No. : 91-40-23741080, 23740591

9. Following declaration was given by the inventor(s)

We the true and first inventors for the invention or the applicant(s) in the convention country declare that the applicant(s) herein are our assignee or legal representative:

(a) ALURI PHANINDRUDU

(b) ASHISH GOGIA

10. That to the best of our knowledge, information and belief the fact and matters stated herein are correct ad that there is no lawful ground of objection to the grant of patent to us on this application.

11. Following are the attachment with the application: -

(a) Complete Specification (3 copies).

(b) Drawings (NIL)

(c) Priority document(s)

(i) Fee Rs. 6000/- in Bank Draft bearing No 020564 dated 28-08-03 on State Bank of Hyderabad.

We request that a Patent may be granted to us for the said invention.

Dated this 22nddday of November 2003.

AUROBINDO PHARMA LTD. INDIA HYDERABAD

(D.V. SIVAKUMARAN)
DIRECTOR

TO
THE CONTROLLER OF PATENTS,
THE PATENT OFFICE,
CHENNAI

THE PATENT ACT, 1970

COMPLETE

SPECIFICATION

(SECTION 10)

TITLE

"PHARMACEUTICAL COMPOSITIONS OF ANHYDROUS MIRTAZAPINE"

APPLICANT

AUROBINDO PHARMA LIMITED
HAVING REGISTERED OFFICE AT
PLOT NO.2, MAITRIVIHAR COMPLEX,
AMEERPET, HYDERABAD – 500 038
INDIA, AN INDIAN ORGANIZATION

The following specification particularly describes and ascertains the nature of this invention and the manner in which the same is to be performed.

BACKGROUND OF THE INVENTION

This invention is in the general field of pharmaceuticals and relates in particular to the formulation of Mirtazapine or any of its pharmaceutically acceptable salts. More specifically, the present invention relates to a pharmaceutical composition, which comprises anhydrous Mirtazapine or any of its pharmaceutically acceptable salts as an active ingredient with other suitable excipients.

Mirtazapine, 1,2,3,4,10,14b-hexahydro-2-methyl-pyrazino [2,1 -a]pyrido[2,3-c][2] benzazepine, is approved, under the trademark Remeron.RTM., by the U.S. Food and Drug Administration, for the treatment of depression. Mirtazapine has a tetracyclic chemical structure unrelated to other classes of antidepressants such as selective serotonin reuptake inhibitors, tricyclics, or monoamine oxidase inhibitors.

U.S. Pat. No. 4,062,848, claims a class of tetracyclic compounds in which Mirtazapine is a member and discloses a process for making Mirtazapine. US Pat no 6552189 claims a method of preparation of low-hygroscopic anhydrous Mirtazapine crystals from the hydrate form of Mirtazapine by the methods of pulverization and drying. US Patent application no 20030130504 claims anhydrous Mirtazapine crystals having a water-content of not more than 0.5% by weight. But nowhere in any of the above prior art --- formulations and the compositions of anhydrous Mirtazapine are disclosed or claimed.

In accordance with the present invention, anhydrous Mirtazapine is prepared as pharmaceutical compositions that are particularly useful for the treatment of depression. Such compositions comprise a therapeutically effective amount of anhydrous Mirtazapine with pharmaceutically acceptable carriers and/or excipients known to one of skill in the art.

DETAILED DESCRIPTION OF THE INVENTION

Owing to certain handling advantages that anhydrous Mirtazapine has over the other forms of Mirtazapine, formulation of the same with some suitable adjuvants is contemplated and achieved in our lab with satisfactory results in terms of the formulation parameters which constitute both invitro as well as invivo aspects.

The different kinds of excipients that can be used for the above formulation are selected from binders, lubricants, disintegrants, fillers and etc

In the present specification, the term "anhydrous" of the anhydrous Mirtazapine crystals means that the Mirtazapine crystals do not substantially contain moisture.
Those skilled in the art will recognize, or be able to ascertain using simple routine experimentation, many equivalents to the specific embodiments of the invention described in the present specification. Such equivalents are intended to be encompassed in the scope of the present invention as recited in the following claims.

Goal of this invention is to formulate water insoluble drug anhydrous Mirtazapine in such a way that it will comply with the reference product [usually innovator's REMERON] in terms of invivo parameters like bioequivalence and invitro parameters like dissolution, disintegration and etc. This invention also aims to address particular difficulties associated with dealing with Mirtazapine hemihydrate and provide a simple, cost effective and efficient formulation of anhydrous Mirtazapine on a commercial scale.

EXAMPLES

The present invention will now be further explained in the following example. However, the present invention should not be construed as limited thereby. One of ordinary skill in the art will understand how to vary the exemplified preparations to obtain the desired results.

It should be understood that some modification, alteration and substitution is anticipated and expected from those skilled in the art without departing from the teachings of the invention. Accordingly, it is appropriate that the following claims be construed broadly and in a manner consistent with the scope and spirit of the invention.

Example

S. No.	Ingredients	w/w% per Tablet
1.	Mirtazapine	Equivalent to Mirtazapine 7.5/15/30/45 mg
2.	Lactose Monohydrate	63.00-73.00%
3.	Hydroxypropyl Cellulose	1.5-3.5%
4.	Starch	6.5-8.5%
5.	Colloidal Silicon Dioxide	0.54-1.54%
6.	Low-substituted Hydroxypropyl Cellulose	6.5-8.5%
7.	Magnesium Stearate	0.26-0.66%
8.	Opadry Yellow	2.0-4.0%
9.	Purified Water	q.s

The different formulation processes that can be employed for making the disclosed formulation are by dry granulation, wet granulation, slugging, compaction, direct compression and etc. But preferably the above tablets are prepared by the conventional wet granulation formulation process, which is very well known in the filed of formulations. The different process steps that are involved in this method are sifting, mixing, granulating, drying, sizing the granules, lubricating and finally compressing the granulates into the tablets and optionally film coating the core.

With regard to the invention disclosed here, it will be obvious that the same may be varied in many ways. Such variations are not to be regarded as a departure from the spirit and scope of the invention and all such modifications are intended to be included within the scope of the claims.

CLAIMS

We claim:

[1] A pharmaceutical composition comprising anhydrous Mirtazapine or any of its pharmaceutically acceptable salts as an active along with suitable excipients.

[2] Anhydrous Mirtazapine as claimed in claim 1 is a crystalline material having particle size 90% less than 400 Microns.

[3] Pharmaceutical formulation process for the composition as claimed in claim 1 is by any granulation or Direct Compression method.

[4] Pharmaceutical formulation process as claimed in claim 3 is wet granulation process.

[5] A pharmaceutical composition as described in claim [1] wherein the dosage form is a tablet.

[6] A pharmaceutical formulation as claimed in claim 1 is bioequivalent to reference product and is stable for a shelf life of 24 months.

[7] A pharmaceutical composition as described in claim [1] wherein the dosage form is an Orally dissolving tablet.

Dated this the 19th day of November 2003

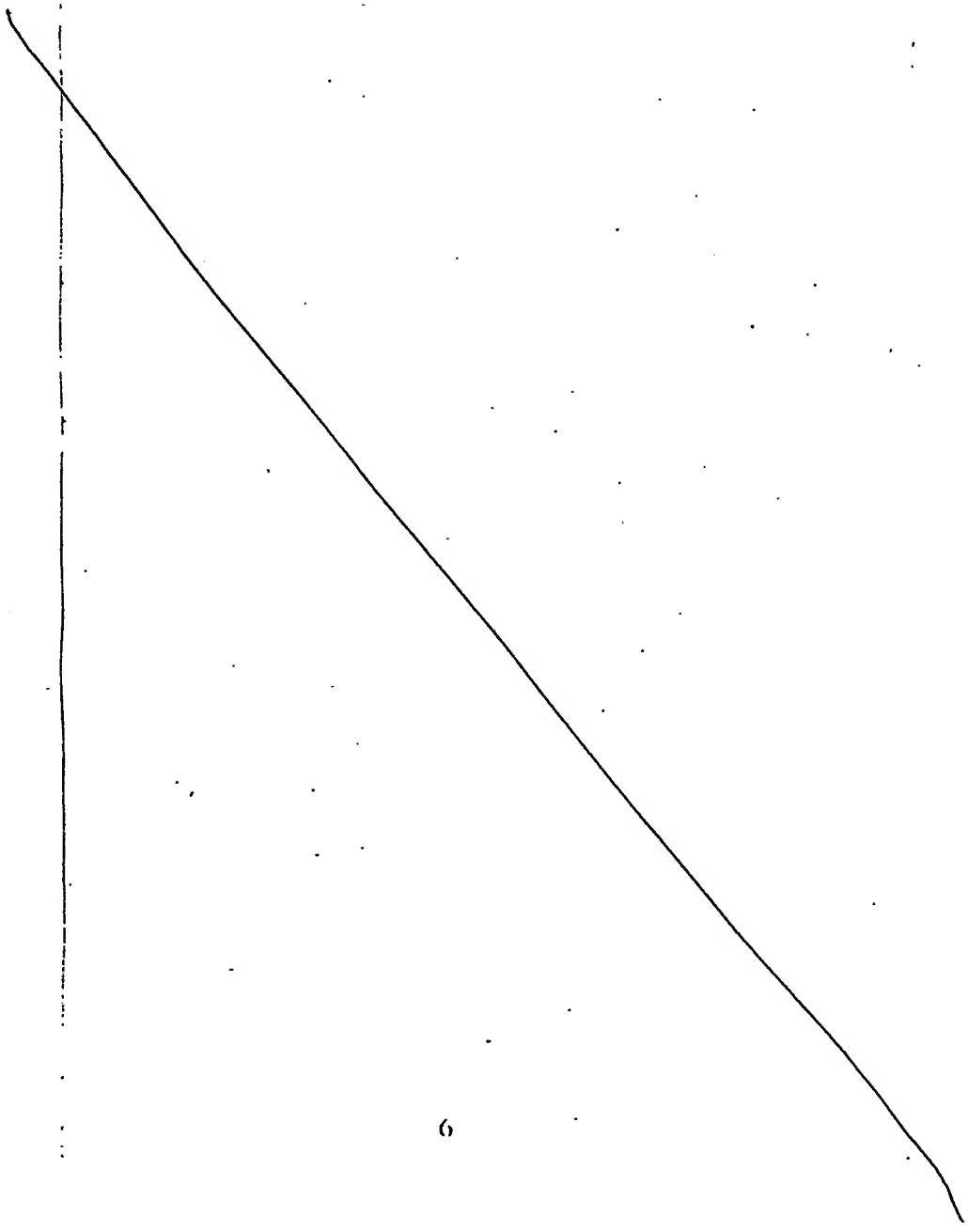
Aurobindo Pharma Limited

Nanda Bhaskara

Ms.Nanda Bhaskara
LEGAL OFFICER
FOR THE APPLICANTS.

ABSTRACT

The present invention relates to Mirtazapine formulations containing anhydrous Mirtazapine as the active, having satisfactory handling properties and which formulation with suitable adjuvants results in pharmaceutical compliance with the reference product in terms of in-vivo parameters like bio-equivalence and etc



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